

APPENDIX 7: P. Josset, B. Pellosse, H. Saraux: Interet d'une solution isotonique amphotere dans le traitement precoce des brulures chimiques corneo-conjunctivales: etude experimentee et histologique [Interest of an isotonic amphoteric solution in the early treatment of corneal-conjunctival base chemical burns: Experimental and histological study].

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ABSTRACT

Treatment of conjunctival-corneal burns with water and buffered isotonic solutions were not shown to be superior to buffered isotonic solutions (amphoteric) or other methods of lavage from the point of view of the intra- and extra-ocular pH or of the endothelial cells.

I - INTRODUCTION

The lesions caused by ocular splashes with strong bases are often followed by severe and dramatic consequences.

These accidents frequently occur in industrial settings where large quantities of sodium hydroxide or ammonia are handled.

In this field, the authors have search to determine the more efficacious methods for the immediate treatment of ocular burns that occur despite mandatory wearing of safety glasses.

Two systems are currently utilized: an eyewash system based on the use of a bottle attached to an eyepiece which delivers a buffered or non-buffered isotonic artificial tears solution or otherwise water rinsing in an eyewash fountain or in a shower adapted for washing the body and the eyes.

In France, simple water rinsing is currently generally recommended, in spite of results with this method that are somewhat disappointing, and in spite of several studies from other countries which have demonstrated the interest of lavage with isotonic and buffered solutions.

This is the reason why the authors undertook this experimental study in order to verify the good outcome with this treatment.

II. REACTION OF THE EYE IN CONTACT WITH BASES

The cornea that is the principal object of this study has a semipermeable membrane in osmotic equilibrium with the intra-ocular fluid and the tears. The presence of foreign molecules sets in motion a disequilibrium and creates a flux of material which that to reestablish the osmotic equilibrium.

In this fashion, a flux of ionic and proteinaceous constituents is established from the hypertonic locus toward the hypotonic locus, and a flux of the solvent and of constituents not contained in the hypertonic solution in a contrary manner. In chemical burns, the phenomena of osmotic migration becomes of importance in cutaneous and tissue necrosis and it can be observed in large burns immersed in hypotonic solutions (water) that there is enormous swelling which places the patient's life in danger.

In contact with tissues, strong bases manifest the potentialities of the OH^- ion that can rapidly penetrate into the tissues by protein catalysis and binding to H^+ ions causing tissue coagulation, in this manner slowing its own penetration.

Whatever the quantity of base splashed on the face, the amount which contact the eye is significantly reduced taking into account on one hand the small surface area of the eye and on the other hand the palpebral reflex which wipes away surplus liquid so that the volume that remains in the eye can be estimated at about 0.2 ml.

III. DECONTAMINATION METHODS

The authors have considered only the methods of decontamination in first aid that can be found at the site of the accident or are accessible during the first few minutes. In effect, the action of bases is extremely rapid and by 5 minutes their penetration is complete and the lesions have developed.

Two methods are widely used at the present time:

- lavage with large quantities of water based on the effects of dilution and mechanical rinsing
- lavage with buffered isotonic artificial tears solutions.

Dilution with water has as its goal to determine the effect of OH^- ions in proportion to their concentration.

To change a 0.2 ml quantity of 1 N sodium hydroxide from a pH of 14 to a pH of 7, it theoretically requires 1,000 liters of water. Fortunately, the effects of mechanical rinsing reduce these volumes to lesser quantities, but this explains the slowness of the action of water. The principle problem with water is its hypotonicity: it penetrates in effect by osmotic effect into the stroma and with it carries particles of sodium hydroxide which causes edema and lesions of the endothelial cells.

Dilution with isotonic artificial tears solutions has the advances of regulating the osmotic pressure and thus preventing continued penetration of the OH^- ion into the interior of the eye.

Neutralization with buffered solutions.

Buffered solutions are amphoteric compounds having acidic and basic characteristics and a pH very close to neutral (6.5 to 7.5). These solutions are very interesting for neutralization and the quantities required are very small, such that in the case previously cited of 1 N sodium hydroxide, it would only require 1 ml of an active anti-base solution to attain a pH of 7; moreover, it is possible to render these solutions isotonic which combines the two advantages.

It must be emphasized that neutralization with a buffered amphoteric solution is accompanied with only a very small generation of heat, at the limits of measurability (about 0.5 degree C during neutralization of 1 ml of 1 N sodium hydroxide with an anti-sodium hydroxide solution necessary to return the pH to 7).

IV. MATERIALS AND METHODS

The authors have carried out a series of studies on lesions caused by sodium hydroxide in the eye as a function of different methods of ocular lavage.

These studies have been carried out in fifty-five albino rabbits divided into four groups:

- the first and second groups of 13 rabbits each were used for the study of histological lesions.
- the third and fourth groups were used for the study of histological lesions, but also for

measurement of extra- and intra-ocular pH in the anterior chamber.

Ocular burns in the three latter groups were produced with a 1 cm diameter piece of filter paper soaked in 1 N sodium hydroxide and drained which was then applied for 30 seconds into the eye of the animals which were anesthetized with ether and after the loss of the corneal reflex.

Immediately after removal of the filter paper carrying the caustic agent, the eye was washed with running water using a special small shower and with two solutions: 1) an isotonic artificial tears solution (Lav'oeil, solution de lavage Soc-Prevor); and 2) a buffered isotonic product called solution anti-sodium hydroxide (Lav'oeil solution anti-soude Soc-Prevor).

In the third group the pH of the tears was measured at regular intervals until the animals were sacrificed.

In the last group measurements of the extra-ocular and intra-ocular pH were measured by puncture of the anterior chamber that was done at the time of sacrifice. Animals were sacrificed at times from 3 minutes to 24 hours after the ocular burn was induced.

This protocol covered the time that is needed for an injury to develop, with or without the provision of early first aid measures.

V. RESULTS

1. pH Measurements

Measurements of pH were done with Merck reactive paper allowing graduated readings of 0.2 to 0.2 units.

The extra-ocular pH was measured directly by placing the pH paper in the conjunctival cul-de-sac. The pH of the aqueous humor was measured by puncture of the anterior chamber at the time when the animal was sacrificed. This measurement was only done once for each tested eye because taking repeated samples of the anterior chamber fluid has detectable effects on the OH⁻ ion concentration and in consequence on the pH of the anterior chamber.

This anterior chamber puncture makes available a quantity of fluid sufficient for several measurements with the reactive pH paper offering several indicators of varied colors that allows a very reliable reading of the results.

a) Measurement of extra-ocular pH

The measurements displayed in Figure 1 demonstrate that the return to a normal pH is very slow with water, much faster with the isotonic solution, and almost instantaneous with the buffered isotonic solution.

Theoretical calculations demonstrate that the return to a normal pH with the buffered solution takes only one second, while in the authors' studies this result occurs over about 10 seconds (Figure 1).

b) Measurements of intra-ocular pH

Figure 2 displays the results obtained showing that at about three minutes after the burn the pH is 8 with the isotonic solutions and 8.7 with water. Thereafter the pH decreases to reach an area of normal pH in 30 seconds with the isotonic solutions and 4 hours with water. The

buffered isotonic solution produced a less rapid increase and a more rapid and greater decrease with a slow rebound characteristic of a normalization curve.

It is interesting to also incline towards the levels at the onset which allow an explanation of the histological lesions described below, when water is utilized, this demonstrates that very elevated levels of pH are reached which are responsible for the destruction of the epithelial cells. Even if the water lavage is continued for a very prolonged time it is this early increase that leads to the final prognosis.

2. HISTOLOGY

The 1 N concentration of sodium hydroxide used always destroyed the surface epithelium and regardless of the decontamination solution utilized it was not possible to prevent this immediate destruction during the application of the caustic material.

All groups thus developed epithelial ulceration over the first few minutes.

The underlying stroma separated from the epithelium by Bowman's membrane showed variable edema depending on the solution utilized: it appeared major with water and visible with isotonic and buffered isotonic solutions, but less significant.

This edema was clearly due to penetration of the caustic liquid into the interior of the cornea, but above all to alteration of the function of the endothelial cells which being situated in the posterior portion of the stroma have a role in "pumping" the fluids which bathe them.

The anterior portion of the stroma develops modification of its staining properties proportional to chemical and physical properties which most resemble coagulant lesions such as are observed in thermal lesions and it appears likely that measurements where the sodium hydroxide contacts the eye causes release of heat as in all irreversible chemical reactions.

Preliminary studies have demonstrated that in the case of lavage with water there is complete destruction of the endothelial cells whose debris may be seen floating in the anterior chamber.

When the eye is lavaged with an isotonic artificial tears solution, a portion of the endothelial cells survive and demonstrate cytoplasmic swelling lesions corresponding to the extent of the edema, but a significant number survive.

Finally when lavage is done with the buffered isotonic solution, the endothelial cells develop several morphologic variations but their numbers are only slightly diminished.

This large number of surviving cells plays a very important role in the recovery of the functional capacity of the cornea and the studies reported here appear to demonstrate as well a more rapid regrowth of the corneal epithelium, which is explained by the re-establishment of normal corneal function favoring epithelial regrowth.

DISCUSSION

It could appear surprising at first glance to call into question the dogma of ocular lavage with water, however physical-chemical evidence has previously argued in favor of the use of a buffered isotonic solution of artificial tears. The results reported here clearly confirm this point of view, and it is useful to recall that various authors have shown that the use of an isotonic solution minimizes the endothelial cell lesions and is associated with improved cellular regeneration. In the studies performed, isotonic solutions have been used either by external application or by lavage of the anterior

chamber (Bennett, Korey).

These authors have also demonstrated that it is important to intervene within a half-hour following the burn.

The results presented here suggest that it is necessary to intervene as soon as possible and above all within the first few minutes.

Measurements of pH demonstrate that it requires about a half-hour for the pH to return to a near-normal value with isotonic solutions while it requires about four hours to obtain the same result with water.

At this time, the results can be explained by the uptake and penetration of the sodium hydroxide into the eye which is promoted by the movement of fluid towards the interior of the eye, and also by the weak neutralizing capacity of water such that it requires gigantic quantities of water in proportion to isotonic solutions, buffered or not.

CONCLUSION

The studies conducted in the first few minutes and hours following an ocular burn with sodium hydroxide demonstrate that the utilization of an isotonic solution and especially a buffered isotonic solution very rapidly re-establish a physiological extra - and above all intra-ocular pH and preserve a large quantity of endothelial cells which are destroyed when the eye is lavaged with running water.

It thus seems certain that the use of a buffered isotonic solution provides the best chance of preserving a normal ocular function in the course of accidental chemical ocular burns.

REFERENCES

[See French original]